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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,893	07/22/2002	David M Stern	59472-A-PCT-US/JPW/FHB	2372

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Cooper & Dunham
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
EMCH, GREGORY S	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/049,893	STERN ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,45,55-57 and 59-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,45,55-57 and 59-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 21 September 2006 has been entered.

Response to Amendment

Claim 42 has been amended as requested in the amendment filed on 21 September 2006. Following the amendment, claims 42, 45, 55-57 and 59-70 are pending in the instant application.

Claims 42, 45, 55-57 and 59-70 are under examination in the instant office action.

The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Claims 42, 45, 55-57 and 59-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims, as amended, are to directed to a method for preventing and/or treating a disease involving β-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a compound other than sRAGE, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE, wherein the β-sheet fibril is formed from an amyloid-β peptide selected from the group consisting of Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, so as to thereby prevent and/or treat a disease involving β-sheet fibril formation other than Alzheimer's Disease in the subject.

Applicants are required to cancel the new matter in the response to this Office action. Alternatively, Applicants are invited to identify sufficient written support in the original specification for the "limitations" indicated above. Applicants' remarks, in the Response filed 21 September 2006 do not provide sufficient direction for the written description for the above-mentioned limitation of claims 42, 45, 55-57 and 59-70. Here, Applicants assert, "Support for amended claim 42 can be found in the specification at, *inter alia*, page 40, lines 14 and 15."

Accordingly, it is noted that p.40, lines 14 and 15 of the specification originally discloses, "In one embodiment, the compound is sRAGE or a fragment thereof." Therefore, the only compounds that are contemplated as comprising sRAGE are: 1) the full-length sRAGE, or 2) a fragment of the full-length sRAGE. Nowhere in the specification is there any mention of "a compound other than sRAGE, which compound comprises a fragment of sRAGE." There is no written support for this limitation, and it is thus considered to be new matter.

Double Patenting

The provisional obviousness-type double patenting rejections of claims 42, 45, 55-57 and 59-70 as being unpatentable over claims 1-3 and 16 of copending Application No. 08/905,709 and claims 36, 39, 40 and 53 of copending Application No. 09/498,459 are maintained for reasons of record.

In the reply filed 21 September 2006, it is stated that Applicants will respond to the rejection once it is no longer provisional. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 102

The rejection of claims 42, 45, 55, 57, 59-61, 63-68 and 70 under 35 U.S.C. 102(b) as being anticipated by WO 97/26913 to Stern et al. is maintained for reasons of record and as set forth *infra*.

The claims are to directed to a method for preventing and/or treating a disease involving β-sheet fibril formation, other than Alzheimer's Disease, in a subject which

comprises administering to the subject a binding-inhibiting amount of a compound other than sRAGE, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE, wherein the β-sheet fibril is formed from an amyloid-β peptide selected from the group consisting of Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, so as to thereby prevent and/or treat a disease involving β-sheet fibril formation other than Alzheimer's Disease in the subject.

In the reply filed 21 September 2006, Applicants assert that the '913 application fails to teach methods reciting a compound *other than sRAGE*, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE (page 7 of the Response). Accordingly, Applicants maintain that '913 application fails to teach each and every element of independent claim 42.

Applicants' argument has been fully considered and is not found persuasive.

The '913 document at p.10, lines 28-29 teaches, "The agent may be a soluble receptor for advanced glycation end product" i.e., sRAGE. The '913 document also teaches that the agent may be "a soluble extracellular portion of a receptor for advanced glycation end product" (p.10, lines 28-29), i.e., a fragment of sRAGE, thus meeting the claimed limitation of "a compound *other than sRAGE*, which compound comprises a fragment of sRAGE."

Also, as stated previously, the '913 document teaches a method for treating a subject with a condition associated with interaction of an amyloid-β peptide with a receptor for advanced glycation endproduct (RAGE), which comprises administering to the subject an agent capable of inhibiting the interaction between the amyloid β-peptide

and RAGE, the agent being present in an amount effective to inhibit the interaction between the amyloid β-peptide and RAGE, thereby treating the subject (p.12, lines 19-27). The '913 document also teaches that the condition may be a number of disorders, e.g. diabetes, renal failure, hyperlipidemic atherosclerosis, ALS, neuronal cytotoxicity, MS, Down's syndrome, neuronal degeneration (p.12, lines 29-33). Also, the condition may be associated with amyloid β-peptide fibril or with aggregation of amyloid β-peptide (p.13, lines 5-6) and Aβ (1-40) is taught (p.20, line 10).

Although the '913 document patent did not specifically teach the species of: Aβ (1-39), Aβ (1-42) and Aβ (1-40) Dutch variant, one of skill in the art would know that the disclosed "amyloid β-peptide" encompasses these species (see, for example, WO 99/27944 to Schenk et al. at p.14, lines 25-28; or Hardy, Amyloid, the presenilins and Alzheimer's disease, Trends Neurosci. 1997 Apr; 20(4): 154-158). These references explicitly teach that the naturally occurring amyloid β-peptides in humans include Aβ (1-39), Aβ (1-40), Aβ (1-42), and Aβ (1-40) Dutch variant. Thus, the limitations of claims 42, 45, 55, 57, 63-68, and 70 have been met by the '913 document.

Furthermore, the document teaches that the subject may be a mammal or human (p. 12, lines 33-34), and the administration may be intralesional, intraperitoneal, intramuscular, intravenous, liposome-mediated delivery, topical, nasal, oral, anal, ocular or otic delivery (p.12, line 34 – p.13, line 1), thus meeting the limitations of claims 59-61.

Thus contrary to Applicants' assertions, the '913 document teaches all the elements of the claims. Accordingly, claims 42, 45, 55, 57, 59-61, 63-68 and 70 are anticipated by Stern et al.

The rejection of claims 42, 45, 55, 57, 59-68 and 70 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,864,018 to Morser et al. is maintained for reasons of record and as set forth *infra*.

The claims are to directed to a method for preventing and/or treating a disease involving β-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a compound other than sRAGE, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE, wherein the β-sheet fibril is formed from an amyloid-β peptide selected from the group consisting of Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, so as to thereby prevent and/or treat a disease involving β-sheet fibril formation other than Alzheimer's Disease in the subject.

In the reply filed 21 September 2006, Applicants assert that the '018 patent fails to teach the claimed methods because the patent fails to teach methods reciting an amyloid-β peptide selected from the group consisting of Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant (page 8 of the Response). Accordingly, Applicants maintain that '913 application fails to teach each and every element of independent claim 42.

Applicants' arguments have been fully considered and are not found persuasive.

The '018 patent discloses that the isolated polypeptides of the invention comprise those "related to and/or derived from soluble human RAGE polypeptides," i.e., sRAGE. In addition, the '018 patent teaches, "soluble RAGE polypeptides generally comprise

fragments of the extracellular domain of RAGE" (col.5, lines 4-38) i.e., a fragment of sRAGE. Thus, since fragments of sRAGE are explicitly taught, the claimed limitation of "a compound *other than sRAGE*, which compound comprises a fragment of sRAGE" is met by the '018 patent.

Also, as stated previously, the '018 patent discloses a method for inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to said subject a polypeptide which comprises a soluble extracellular portion of a receptor for advanced glycation endproduct (AGE) or a derivative thereof, said polypeptide being capable of inhibiting an interaction between amyloid β-peptide and RAGE. The '018 patent also discloses compositions for blocking interaction between AGE and RAGE. Such compositions may be used to reduce the pathological effects of diabetes (col.4, lines 10-34, 54-64; col.19, lines 9-15). The interaction of AGEs with RAGE has been implicated in activation of microglial cells by amyloid β-peptide (col. 19, lines 15, 16). The β-sheet fibril is defined by the instant specification as comprising amyloid fibril, prion-derived fibril, or amyloid-β peptide (p.26, lines 22-24). Thus, a compound capable of blocking the interaction of amyloid-β peptide and RAGE would inherently be capable of blocking the interaction between a β-sheet fibril and RAGE. Thus, the limitations of claims 42, 45, 55, 57 and 70 have been met by the '018 patent.

Although the '018 patent did not specifically teach the species of: Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, one of skill in the art would know that the disclosed "amyloid β-peptide" encompasses these species (see, for example, WO 99/27944 to Schenk et al. at p.14, lines 25-28; or Hardy, Amyloid, the presenilins and

Alzheimer's disease, Trends Neurosci. 1997 Apr; 20(4): 154-158). These references explicitly teach that the naturally occurring amyloid β-peptides in humans include Aβ (1-39), Aβ (1-40), Aβ (1-42), and Aβ (1-40) Dutch variant. Therefore, since the Morser et al. patent discloses amyloid-β peptide, said peptide would inherently include at least one of the species recited by the instant claim 42 and dependent claims.

The '018 patent discloses administration of the polypeptides to human and non-human patients (col.18, lines 64-67; col.19, lines 1-31), thus meeting the limitations of claims 59 and 60. Further, the patent discloses that the a method of administration may be selected from oral, intravenous, intraperitoneal, intramuscular, or local administration (col.19, lines 57-67), thus meeting the limitations of claim 61. The '018 patent discloses prevention or treatment of disorders, such as Diabetes Mellitus, diabetic macrovasculopathy (atherosclerosis), neuropathy, nephropathy, occlusive vascular disorders, amyloidosis (col.19, lines 6-24), thus meeting the limitations of claims 62-68.

Thus contrary to Applicants' assertions, the '018 patent discloses all the elements of the claims. Accordingly, claims 42, 45, 55, 57-68 and 70 are anticipated by Morser et al.

Claim Rejections - 35 USC § 103

The rejection of claims 42, 45, 55-57 and 59-70 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,864,018 to Morser et al., in view of Lilley et al., further in view of Kelley is maintained for reasons of record and as set forth *infra*.

The claims, as amended, are to directed to a method for preventing and/or treating a disease involving β-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a compound other than sRAGE, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE, wherein the β-sheet fibril is formed from an amyloid-β peptide selected from the group consisting of Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, so as to thereby prevent and/or treat a disease involving β-sheet fibril formation other than Alzheimer's Disease in the subject.

In the reply filed 21 September 2006, Applicants assert that the combination of the '018 patent, Lilley et al. and Kelley fail to teach or suggest all the elements of the claimed methods. Applicants also assert, "Nowhere does the '018 patent teach or suggest a method for preventing and/or treating a disease involving β-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a *compound comprising a fragment of sRAGE, but not sRAGE, wherein the* β-sheet fibril is formed from an amyloid-β peptide selected from the group consisting of Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant." Applicants also assert that Lilley et al. and Kelley fail to cure this deficiency, in that combined, they also fail to teach or suggest the claimed method (pages 9 and 10 of the Response).

Applicants' arguments have been fully considered and are not found persuasive.

The '018 patent discloses that the isolated polypeptides of the invention comprise those "related to and/or derived from soluble human RAGE polypeptides," i.e., sRAGE.

In addition, the '018 patent teaches, "soluble RAGE polypeptides generally comprise fragments of the extracellular domain of RAGE" (col.5, lines 4-38) i.e., a fragment of sRAGE. Thus, since fragments of sRAGE are explicitly taught, the claimed limitation of "a compound *other than sRAGE*, which compound comprises a fragment of sRAGE" is met by the '018 patent.

Also, as stated previously, the '018 patent discloses a method for inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to said subject a polypeptide which comprises a soluble extracellular portion of a receptor for advanced glycation end product (AGE) or a derivative thereof, said polypeptide being capable of inhibiting an interaction between amyloid β-peptide and RAGE. The '018 patent also discloses compositions for blocking interaction between AGE and RAGE. Such compositions may be used to reduce the pathological effects of diabetes (col.4, lines 10-34, 54-64; col.19, lines 9-15). The interaction of AGEs with RAGE has been implicated in activation of microglial cells by amyloid β-peptide (col. 19, lines 15, 16). The β-sheet fibril is defined by the instant specification as comprising amyloid fibril, prion-derived fibril, or amyloid-β peptide (p.26, lines 22-24). Thus, a compound capable of blocking the interaction of amyloid-β peptide and RAGE would inherently be capable of blocking the interaction between a β-sheet fibril and RAGE. Thus, the limitations of claims 42, 45, 55, 57 and 70 have been taught by the '018 patent.

Although the '018 patent did not specifically teach the species of: Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, one of skill in the art would know that the disclosed "amyloid β-peptide" encompasses these species (see, for example, WO

99/27944 to Schenk et al. at p.14, lines 25-28; or Hardy, Amyloid, the presenilins and Alzheimer's disease, Trends Neurosci. 1997 Apr; 20(4): 154-158). These references explicitly teach that the naturally occurring amyloid β-peptides in humans include Aβ (1-39), Aβ (1-40), Aβ (1-42), and Aβ (1-40) Dutch variant. Therefore, since the Morser et al. patent discloses amyloid-β peptide, said peptide would inherently include at least one of the species recited by the instant claim 42 and dependent claims.

The '018 patent discloses administration of the polypeptides to human and non-human patients (col.18, lines 64-67; col.19, lines 1-31), as in claims 59 and 60. Further, the patent discloses that the a method of administration may be selected from oral, intravenous, intraperitoneal, intramuscular, or local administration (col.19, lines 57-67), as in claim 61. The '018 patent discloses prevention or treatment of disorders, such as Diabetes Mellitus, diabetic macrovasculopathy (atherosclerosis), neuropathy, nephropathy, occlusive vascular disorders, amyloidosis (col.19, lines 6-24), as in claims 62-68.

The '018 patent does not disclose treating a wound associated with diabetes. However, Kelley teaches that prion diseases result from β-sheets fibril formation (abstract), as in claim 56.

Neither the '018 patent nor Kelley teaches a prion-derived fibril. However, Lilley et al. teaches that diabetes mellitus is associated with delayed wound healing (abstract), as in claim 69.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the

methods of treating atherosclerotic plaque formation in a diabetic subject disclosed by U.S. Patent No. 5,864,018 to Morser et al. with treating a prion disease as taught by Kelley and treating wounds associated with diabetes as taught by Lilley et al. The person of ordinary skill in the art would have been motivated to make these modifications in order to treat more of the complications associated with diabetes as taught by the '018 patent (col. 19, lines 6-24) and because compounds that prevent prion particle formation are important for therapeutics as taught by Kelley (p.932). The person of ordinary skill in the art would have had a reasonable expectation of success because the '018 patent teaches that the methods would work (entire document).

Thus, contrary to Applicants' assertions, the combination of the prior art references is deemed proper. Accordingly, claims 42, 45, 55-57 and 59-70 are unpatentable over to Morser et al., in view of Lilley et al., further in view of Kelley.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 9AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
04 December 2006

ELIZABETH KEMMERER
PRIMARY EXAMINER